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NEWS	3	DEC 18	CA/CAPLUS pre-1967 chemical substance index entries enhanced with preparation role
NEWS	4	DEC 18	CA/CAPLUS patent kind codes updated
NEWS	5	DEC 18	MARPAT to CA/CAPLUS accession number crossover limit increased to 50,000
NEWS	6	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS	7	DEC 27	CA/CAPLUS enhanced with more pre-1907 records
NEWS	8	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	9	JAN 16	CA/CAPLUS Company Name Thesaurus enhanced and reloaded
NEWS	10	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	11	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	12	JAN 22	CA/CAPLUS updated with revised CAS roles
NEWS	13	JAN 22	CA/CAPLUS enhanced with patent applications from India
NEWS	14	JAN 29	PHAR reloaded with new search and display fields
NEWS	15	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS	16	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS	17	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS	18	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS	19	FEB 26	MEDLINE reloaded with enhancements
NEWS	20	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS	21	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS	22	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS	23	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS	24	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS	25	MAR 16	CASREACT coverage extended
NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.		
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=> s (3,4-hydroxy-L-phenylalanine)OR L-Dopa  
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE  
Some commands only work in certain files. For example, the EXPAND  
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FILE COVERS 1907 - 16 Mar 2007 VOL 146 ISS 13  
FILE LAST UPDATED: 15 Mar 2007 (20070315/ED)

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=> s (3,4-hydroxy-L-phenylalanine) or l-dopa  
6842514 3  
5541690 4  
452519 HYDROXY  
11 HYDROXIES  
452530 HYDROXY  
(HYDROXY OR HYDROXIES)  
1549150 L  
79700 PHENYLALANINE  
779 PHENYLALANINES  
80014 PHENYLALANINE  
(PHENYLALANINE OR PHENYLALANINES)  
0 3,4-HYDROXY-L-PHENYLALANINE

(3 (W) 4 (W) HYDROXY (W) L (W) PHENYLALANINE)

1549150 L

16526 DOPA

15 DOPAS

16529 DOPA

(DOPA OR DOPAS)

8760 L-DOPA

(L (W) DOPA)

L1 8760 (3,4-HYDROXY-L-PHENYLALANINE) OR L-DOPA

=> s L1 AND incorporation

203446 INCORPORATION

1036 INCORPORATIONS

203909 INCORPORATION

(INCORPORATION OR INCORPORATIONS)

L2 100 L1 AND INCORPORATION

=> s L2 and unnatural

5053 UNNATURAL

1 UNNATURALS

5053 UNNATURAL

(UNNATURAL OR UNNATURALS)

L3 3 L2 AND UNNATURAL

=> d ti all

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

TI Expanding the eukaryotic genetic code using orthologous aminoacyl-tRNA synthetases genetically engineered for specificity toward non-natural amino acids

AN 2004:934465 CAPLUS

DN 141:389844

ED Entered STN: 06 Nov 2004

TI Expanding the eukaryotic genetic code using orthologous aminoacyl-tRNA synthetases genetically engineered for specificity toward non-natural amino acids

IN Chin, Jason W.; Cropp, Ashton T.; Anderson, Christopher J.; Schultz, Peter G.

PA The Scripps Research Institute, USA

SO PCT Int. Appl., 276 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N

CC 3-2 (Biochemical Genetics)

Section cross-reference(s): 7, 10

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094593	A2	20041104	WO 2004-US11786	20040416
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

- AB This invention provides compns. and methods for producing translational components that expand the number of genetically encoded amino acids in eukaryotic cells. The components include orthogonal tRNAs, orthogonal aminoacyl-tRNA synthetases, orthogonal pairs of tRNAs/synthetases, and unnatural amino acids. Thus, *Escherichia coli* tyrosyl-tRNA synthetase (EcTyrRS) forms an orthogonal pair with the *Bacillus stearothermophilus* tRNA<sup>CUA</sup> in mammalian cells. A general approach for the isolation of aminoacyl-tRNA synthetases that incorporate unnatural amino acids with high fidelity into proteins in response to an amber codon in *Saccharomyces cerevisiae* is based on the activation of GAL4 responsive reporter genes (HIS3, URA3, or LacZ) by suppression of amber codons between the DNA-binding domain and transcriptional activation domain of GAL4. The optimization of a GAL4 reporter for pos. selection of active EcTyrRS variants is described. A neg. selection of inactive EcTyrRS variants is also developed with the URA3 reporter by use of a small mol. (5-fluoroorotic acid) added to the growth media as a 'toxic allele'. Five amino acids have been incorporated into proteins efficiently, with high fidelity, in response to the nonsense codon TAG in *S. cerevisiae*: p-acetyl-L-phenylalanine, p-benzoyl-L-phenylalanine, p-azido-L-phenylalanine, O-methyl-L-tyrosine, and p-iodo-L-phenylalanine. A highly efficient method for the selective modification of proteins is described, which involves the genetic incorporation of azide or acetylene containing unnatural amino acids into protein in response to the amber nonsense codon; these amino acid side chains can then be modified by a Huisgen [3+2] cycloaddn. reaction.
- ST genetic code expansion aminoacyl tRNA synthetase genetic engineering;  
tyrosyl tRNA synthetase engineering genetic code *Saccharomyces*;  
unnatural amino acid genetic code tRNA synthetase engineering

d ti,abs,ibib,so L3 2-3

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN  
TI Engineering of mutant orthogonal tRNA - aminoacyl tRNA synthetase pairs from Methanococcus jannaschii for incorporation of unnatural amino acids into proteins in vivo  
AB This invention provides compns. and methods for generating components of protein biosynthetic machinery including orthogonal tRNAs, orthogonal aminoacyl-tRNA synthetases, and orthogonal pairs of tRNAs/synthetases. Methods for identifying orthogonal pairs are also provided. These components can be used to incorporate unnatural amino acids into proteins in vivo. Exemplary improvement of orthogonality of a tRNA from Methanococcus jannaschii, mutating tyrosyl tRNA synthetase so that it charges the Methanococcus jannaschii tRNA<sup>Tyr</sup>CUA with O-methyl-L-tyrosine, generating an archeal leucyl-tRNA synthetase pair, and evolution of an aminoacyl-tRNA synthetase using FACS are described. Sequences of exemplary orthogonal tRNAs and orthogonal aminoacyl tRNA synthetases are provided.

ACCESSION NUMBER: 2002:832927 CAPLUS  
DOCUMENT NUMBER: 137:348409  
TITLE: Engineering of mutant orthogonal tRNA - aminoacyl tRNA synthetase pairs from Methanococcus jannaschii for incorporation of unnatural amino acids into proteins in vivo  
INVENTOR(S): Schultz, Peter; Wang, Lei; Anderson, John Christopher; Chin, Jason W.; Liu, David R.; Magliery, Thomas J.; Meggers, Eric L.; Mehl, Ryan Aaron; Pastrnak, Miro; Santoro, Stephen William; Zhang, Zhiwen  
PATENT ASSIGNEE(S): The Scripps Research Institute, USA  
SOURCE: PCT Int. Appl., 170 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002086075	A2	20021031	WO 2002-US12635	20020419
WO 2002086075	A3	20040624		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2444098	A1	20021031	CA 2002-2444098	20020419
US 2003082575	A1	20030501	US 2002-126927	20020419
US 7045337	B2	20060516		
US 2003108885	A1	20030612	US 2002-126931	20020419
US 7083970	B2	20060801		
EP 1456360	A2	20040915	EP 2002-731454	20020419
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004537984	T	20041224	JP 2002-583590	20020419
US 2006063244	A1	20060323	US 2004-2387	20041201
US 2005208536	A1	20050922	US 2004-9635	20041210
US 2005250183	A1	20051110	US 2004-17550	20041217
US 2006233744	A1	20061019	US 2005-254161	20051018

US 2006234367	A1	20061019	US 2005-254170	20051018
PRIORITY APPLN. INFO.:			US 2001-285030P	P 20010419
			US 2002-355514P	P 20020206
			US 2002-126927	A1 20020419
			US 2002-126931	A3 20020419
			WO 2002-US12635	W 20020419

SO PCT Int. Appl., 170 pp.  
CODEN: PIXXD2

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

TI Dose-response relations for unnatural amino acids at the agonist binding site of the nicotinic acetylcholine receptor: tests with novel side chains and with several agonists

AB Structure-function relations in the nicotinic acetylcholine receptor are probed using a recently developed method based on chemical synthesis of nonsense suppressor tRNAs with unnatural amino acid residues, site-directed incorporation at nonsense codons in *Xenopus laevis* oocytes, and electrophysiol. measurements. A broad range of unnatural amino acids, as many as 14 at a given site, are incorporated at three sites,  $\alpha 93$ ,  $\alpha 190$ , and  $\alpha 198$ , all of which are tyrosine in the wild-type receptor and are thought to contribute to the agonist binding site. Confirming and expanding upon earlier studies using conventional mutagenesis, the three tyrosines are shown to be in substantially different structural microenvironments. In particular, a crucial role is established for the hydroxyl group of  $\alpha \text{Tyr}93$ , whereas a variety of substituents are functional at the analogous position of  $\alpha \text{Tyr}198$ . Interestingly, consideration of three different agonists (acetylcholine, nicotine, and tetramethylammonium) does not discriminate between these two best-characterized binding site residues. In addition, double-mutation studies establish the independent effects of mutations at the pore region (second transmembrane region) and at the agonist binding site, and this observation leads to a novel strategy for adjusting EC50 values. These results establish the broad generality and great potential of the unnatural amino acid methodol. for illuminating subtle structural distinctions in neuroreceptors and related integral membrane proteins.

ACCESSION NUMBER: 1996:714935 CAPLUS

DOCUMENT NUMBER: 126:55002

TITLE: Dose-response relations for unnatural amino acids at the agonist binding site of the nicotinic acetylcholine receptor: tests with novel side chains and with several agonists

AUTHOR(S): Kearney, Patrick C.; Nowak, Mark W.; Zhong, Wenge; Silverman, Scott K.; Lester, Henry A.; Dougherty, Dennis A.

CORPORATE SOURCE: Division Biology, California Institute Technology, Pasadena, CA, 91125, USA

SOURCE: Molecular Pharmacology (1996), 50(5), 1401-1412  
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: Williams & Wilkins.

DOCUMENT TYPE: Journal

LANGUAGE: English

SO Molecular Pharmacology (1996), 50(5), 1401-1412  
CODEN: MOPMA3; ISSN: 0026-895X

s L2 and peptide  
366593 PEPTIDE  
268447 PEPTIDES  
469536 PEPTIDE  
(PEPTIDE OR PEPTIDES)  
L4 5 L2 AND PEPTIDE

=> d ti, so, abs, ibib 1-5 L4

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN  
TI Pseudomonas translation system for incorporation of  
non-naturally encoded amino acids into proteins  
SO PCT Int. Appl., 149pp.  
CODEN: PIXXD2  
AB The invention provides methods and compns. for in vivo  
incorporation of non-naturally encoded amino acids into  
polypeptides by Pseudomonas species and strains derived therefrom. The  
Pseudomonas translation system comprises an orthogonal tRNA (O-tRNA) and  
an orthogonal aminoacyl-tRNA synthetase (O-RS). Typically, the O-RS  
preferentially aminoacylates the O-tRNA with at least one non-naturally  
encoded amino acid and the O-tRNA recognizes at lease one selector codon.  
The system is capable of functioning in a Pseudomonas host cell or with  
the translation components of a Pseudomonas cell to provide a polypeptide  
comprising a non-naturally encoded amino acid. The system is exemplified  
by the incorporation of carbonyl group-containing  
p-acetyl-DL-phenylalanine and alkyne-containing propargyl-tyrosine into human  
growth hormone. Also provided are compns. including proteins with  
non-naturally encoded amino acids made by Pseudomonas species and strains  
derived therefrom, said proteins comprising novel reactive residues for  
conjugation with polyethylene glycol derivs.

ACCESSION NUMBER: 2006:1310659 CAPLUS  
DOCUMENT NUMBER: 146:58233  
TITLE: Pseudomonas translation system for  
incorporation of non-naturally encoded amino  
acids into proteins  
INVENTOR(S): Cho, Ho Sung  
PATENT ASSIGNEE(S): Ambrx, Inc., USA  
SOURCE: PCT Int. Appl., 149pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006132969	A2	20061214	WO 2006-US21463	20060602
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2005-687603P P 20050603

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN  
TI Expanding the eukaryotic genetic code using orthologous aminoacyl-tRNA

synthetases genetically engineered for specificity toward non-natural amino acids

SO PCT Int. Appl., 276 pp.

CODEN: PIXXD2

AB This invention provides compns. and methods for producing translational components that expand the number of genetically encoded amino acids in eukaryotic cells. The components include orthogonal tRNAs, orthogonal aminoacyl-tRNA synthetases, orthogonal pairs of tRNAs/synthetases, and unnatural amino acids. Thus, Escherichia coli tyrosyl-tRNA synthetase (EcTyrRS) forms an orthogonal pair with the Bacillus stearothermophilus tRNACUA in mammalian cells. A general approach for the isolation of aminoacyl-tRNA synthetases that incorporate unnatural amino acids with high fidelity into proteins in response to an amber codon in Saccharomyces cerevisiae is based on the activation of GAL4 responsive reporter genes (HIS3, URA3, or LacZ) by suppression of amber codons between the DNA-binding domain and transcriptional activation domain of GAL4. The optimization of a GAL4 reporter for pos. selection of active EcTyrRS variants is described. A neg. selection of inactive EcTyrRS variants is also developed with the URA3 reporter by use of a small mol. (5-fluoroorotic acid) added to the growth media as a 'toxic allele'. Five amino acids have been incorporated into proteins efficiently, with high fidelity, in response to the nonsense codon TAG in S. cerevisiae: p-acetyl-L-phenylalanine, p-benzoyl-L-phenylalanine, p-azido-L-phenylalanine, O-methyl-L-tyrosine, and p-iodo-L-phenylalanine. A highly efficient method for the selective modification of proteins is described, which involves the genetic incorporation of azide or acetylene containing unnatural amino acids into protein in response to the amber nonsense codon; these amino acid side chains can then be modified by a Huisgen [3+2] cycloaddn. reaction.

ACCESSION NUMBER: 2004:934465 CAPLUS

DOCUMENT NUMBER: 141:389844

TITLE: Expanding the eukaryotic genetic code using orthogonal aminoacyl-tRNA synthetases genetically engineered for specificity toward non-natural amino acids

INVENTOR(S): Chin, Jason W.; Cropp, Ashton T.; Anderson, Christopher J.; Schultz, Peter G.

PATENT ASSIGNEE(S): The Scripps Research Institute, USA

SOURCE: PCT Int. Appl., 276 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094593	A2	20041104	WO 2004-US11786	20040416
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:				
BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004233083	A1	20041104	AU 2004-233083	20040416
CA 2520750	A1	20041104	CA 2004-2520750	20040416
US 2004265952	A1	20041230	US 2004-826919	20040416
AU 2004253857	A1	20050113	AU 2004-253857	20040416



CA 2527877	A1	20050113	CA 2004-2527877	20040416
US 2005009049	A1	20050113	US 2004-825867	20040416
WO 2005003294	A2	20050113	WO 2004-US11833	20040416

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1613735	A2	20060111	EP 2004-759917	20040416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
EP 1636340	A2	20060322	EP 2004-785787	20040416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004011475	A	20060725	BR 2004-11475	20040416
US 2006246509	A1	20061102	US 2006-561121	20060523

PRIORITY APPLN. INFO.:

US 2003-463869P	P	20030417
US 2003-479931P	P	20030618
US 2003-493014P	P	20030805
US 2003-496548P	P	20030819
WO 2004-US11786	W	20040416
WO 2004-US11833	W	20040416

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

TI Total Synthesis of Bouvardin, O-Methylbouvardin, and O-Methyl-N9-desmethylbouvardin

SO Journal of the American Chemical Society (1994), 116(19), 8544-56  
CODEN: JACSAT; ISSN: 0002-7863

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Concise total syntheses of bouvardin I and O-methylbouvardin II are described based on the asym. synthesis of  $\beta$ -hydroxy-L-4-iodophenylalanine derivative III (TBDMS = tert-butyldimethylsilyl), its coupling with the selectively protected N,O4-dimethyl-L-DOPA Me ester to provide peptide IV, and subsequent incorporation into a surprisingly successful key Ullmann macrocyclization reaction for preparation of the 14-membered cycloisodityrosine derivative subunit V of the bicyclic hexapeptides. Coupling of V with BocNH-D-Ala-Ala-NMe-Tyr(Me)-Ala-OC6F5 followed by 18-membered-ring macrocyclization strategically conducted with formation of a secondary amide at a D-amino acid amine terminus (C2-N3 amide) provided O-methylbouvardin II. Selective demethylation (BBr3) of II provided bouvardin I in excellent conversion (86%). The extensions of the studies to the preparation of O-methyl-N9-desmethylbouvardin are detailed and its solution-phase conformational properties were examined by 1H NMR in efforts which confirm that the addnl. minor conformation of I and II (ca. 10-15%) observed in nonpolar solvents (CDCl3, THF-d8), arise from a cis N9-C8 N-methylamide conformation.

ACCESSION NUMBER: 1995:55041 CAPLUS

DOCUMENT NUMBER: 122:188112

TITLE: Total Synthesis of Bouvardin, O-Methylbouvardin, and O-Methyl-N9-desmethylbouvardin

AUTHOR(S): Boger, Dale L.; Patane, Michael A.; Zhou, Jiacheng  
CORPORATE SOURCE: Department of Chemistry, Scripps Research Institute,  
La Jolla, CA, 92037, USA  
SOURCE: Journal of the American Chemical Society (1994),  
116(19), 8544-56  
CODEN: JACSAT; ISSN: 0002-7863  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 122:188112

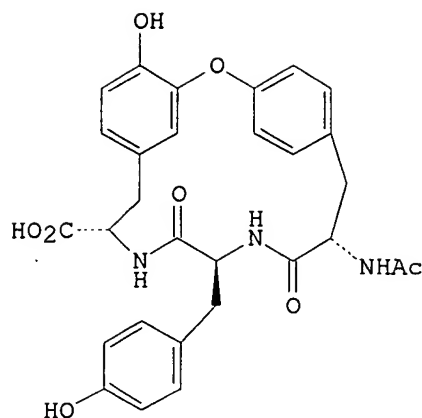
L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN  
TI Total synthesis of L,L-isodityrosine and isodityrosine-derived agents:  
K-13, OF4949-III, and OF4949-IV  
SO Journal of Organic Chemistry (1990), 55(24), 6000-17  
CODEN: JOCEAH; ISSN: 0022-3263  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Full details of the development of reaction conditions for implementation of an activated Ullmann condensation reaction that may be conducted without amino acid racemization and that have proven suitable for incorporation of the selectively protected, functionalized L-Dopa derivs. are described. The application of this procedure in the total synthesis of L,L-isodityrosine, K-13 (I), OF-4949-III and -IV (II, R = H, R1 = Me, H) is detailed. Full details of a study of the macrocyclization reaction required for formation of the 17-membered tripeptides incorporating a diaryl ether linked meta- and paracyclophane structural subunit are provided and illustrate that the cyclization in route to I and II (R = H, OH; R1 = Me, H) is optimally conducted on substrates bearing a carbamate derivative of the C-15/C-9 amine and a C-4 free phenol with C11-N10/C10-N11 amide bond closure.

ACCESSION NUMBER: 1990:612649 CAPLUS  
DOCUMENT NUMBER: 113:212649  
TITLE: Total synthesis of L,L-isodityrosine and  
isodityrosine-derived agents: K-13, OF4949-III, and  
OF4949-IV  
AUTHOR(S): Boger, Dale L.; Yohannes, Daniel  
CORPORATE SOURCE: Dep. Chem. Med. Chem., Purdue Univ., West Lafayette,  
IN, 47907, USA  
SOURCE: Journal of Organic Chemistry (1990), 55(24), 6000-17  
CODEN: JOCEAH; ISSN: 0022-3263  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 113:212649

L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN  
TI Total synthesis of K-13  
SO Journal of Organic Chemistry (1989), 54(11), 2498-502  
CODEN: JOCEAH; ISSN: 0022-3263  
GI



AB A total of K-13 (I), an isodityrosine-derived cyclic tripeptide possessing noncompetitive angiotensin I converting enzyme inhibitory activity, is detailed and is based on the implementation of an activated Ullmann condensation reaction conducted under reaction conditions that permit incorporation of a selectively-protected catechol, including L-Dopa derivs., without amino acid racemization. Studies of the macrocyclization of 17-membered tripeptides incorporating a diaryl ether linked meta- and paracyclophane structural subunit are described.

ACCESSION NUMBER:	1989:232064 CAPLUS
DOCUMENT NUMBER:	110:232064
TITLE:	Total synthesis of K-13
AUTHOR(S):	Boger, Dale L.; Yohannes, Daniel
CORPORATE SOURCE:	Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA
SOURCE:	Journal of Organic Chemistry (1989), 54(11), 2498-502 CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 110:232064

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## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	88972	((Alfonta)OR(Schultz)OR(Zhang)). inv.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/16 19:24
L2	363	L1 AND redox	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/16 19:25
L3	65	L1 AND ((redox)ADJ(active))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/16 19:25
L4	31	L3 AND dopa	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/16 19:26
L5	31	L4 AND unnatural	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/16 19:29
L6	0	L5@pd<"20041118"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/16 19:30
S1	38	(WO 2002/085923)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/16 09:41

## EAST Search History

S2	26	(WO 2002/086075)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/13 12:41
S3	20	(WO 2003/0082575)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/13 12:41
S4	14	(WO 2003/0108885)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/13 12:44
S5	27376	(Redox)AND(Active)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/13 12:45
S6	50	(Redox)ADJ(Active)ADJ(amino)ADJ(acid)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/16 19:23
S7	16	S6 AND (dihydroxy)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	AND	ON	2007/03/13 12:49